REMARKS/ARGUMENTS

Claims 1-39 are pending in the application.

Claims 1-7, 9, 13, 16-20, 26-27, and 29-37 have been amended.

Claims 6-8, 14-15, 21-25, and 38-39 are original claims.

Claim 28 has been canceled without prejudice or waiver.

Claim 28 has been canceled in order to obviate the objection under 37 CFR 1.75 as being a substantial duplicate thereof.

Applicants' have now amended the claims to include the following: "with the proviso that said protein fragments are not ubiquitin fragments and said assay is not a two hybrid assay." It is believed that this proviso renders the 35 USC § 102(b) rejection under Johnsson, et al. moot.

Also, it is further submitted that the combination of cited art under 35 USC § 103 (a) fails to set forth a valid prima facie case of obviousness, and withdrawal of the rejection is requested.

Its is also submitted that the filing of the two terminal disclaimers renders the double patenting rejection moot.

Additionally, withdrawal of the rejection under 35 USC § 102(f) is respectfully requested in view of the declaration under 37 C.F.R. § 1.132.

THE SPECIFICATION

The objection to the original abstract as being too long has been addressed by replacing the original abstract with a new shorter abstract as requested by the Examiner.

ELECTION/RESTRICTION

Applicants' affirm with traverse the election made telephonically on October 14th, 2004. During the telephonic interview Applicants' elected to prosecute the invention of species p53 fused to a reporter fragment, claims 36 and 37, species receptor tyrosine kinase cellular pathway, claim 38 and receptor agonist drug category, claim 39.

CLAIM OBJECTIONS

The objections to claim 16 been addressed by amending the term "Claims" to read –claim--. The objection to claim 35 is now rendered moot by deleting "any one of" as suggested by the Examiner.

THE REJECTIONS UNDER 35 USC § 112 FIRST PARAGRAPH

Claims 6, 9, 19, 20 and 31-35 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Claims 6, 9, 19, 20, and 35 have now been amended to address the rejection by deleting the term "phosphorescent protein".

The rejection of claim 31 has now been addressed by amending the claim to read --fragment—instead of "fragments".

Claims 32-34 have now been amended to so they claim expression vectors that comprise polynucleotides that encode reporter fragments.

THE REJECTIONS UNDER 35 USC § 112 SECOND PARAGRAPH

Claims 13 and 31 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is believed that the amendments to claims 13 and 31 renders the instant rejections moot.

THE REJECTION UNDER 35 USC § 102(b)

The rejection of claims 26-29, and 39 under 35 U.S.C. § 102(b) as being anticipated by Johnson et al. is respectfully traversed. It is respectfully submitted that the newly amended claims which incorporate the language "with the proviso that said protein fragments are not ubiquitin fragments and said assay is not a two hybrid assay" fully distinguishes over the Johnson, et al. reference as well as two hybrid assays previously discussed and successfully argued in the parent and continuing applications.

The strategy of Johnsson et al. for detecting protein-protein interactions is based on the ubiquitin-based split protein sensor (USPS). The strategy relies on cleavage of proteins with N-terminal fusions to ubiquitin by cytosolic proteases (ubiquitinases) that recognize its tertiary structure. The strategy depends on the reassembly of the tertiary structure of the protein ubiquitin from complementary N- and C-terminal fragments and crucially, on the augmentation of this reassembly by oligomerization domains fused to these fragments. Reassembly is detected as specific proteolysis of the assembled product by cytosolic proteases (ubiquitinases). Johnson et al demonstrated that a fusion of a reporter protein-ubiquitin C-terminal fragment could also be cleaved by ubiquitinases, but only if co-expressed with an N-terminal fragment of ubiquitin that

was complementary to the C-terminal fragment. The reconstitution of observable ubiquitinase activity only occurred if the N- and C-terminal fragments were bound through GCN4 leucine zippers. Johnson et al suggested that this "split-gene" strategy could be used as an in vivo assay of protein-protein interactions and analysis of protein assembly kinetics in cells. Clearly, the strategy of Johnson et al. requires additional cellular factors (in this case ubiquitinases) and the detection method does not lend itself to high-throughput screening of cDNA libraries.

THE REJECTION UNDER 35 USC § 103(a)

Claims 26, 36, and 37 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Johnsson et al. in view of Ko et al. Reconsideration of this rejection is courteously requested.

The four factual inquiries that underlie a rejection based 35 USC §103 and which were enunciated by the Supreme Court in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), are first, the scope and content of the prior art are to be determined; second, the differences between the prior art and the claims at issue are to be ascertained; third, the level of ordinary skill in the pertinent art resolved; and fourth, evaluating evidence of secondary considerations.

When the Patent Office applies 35 USC §103, the following tenets of patent law must be adhered to:

(1) the claimed invention must be considered as a whole;

(2) the references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;

(3) the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and

(4) reasonable expectation of success is the standard with which obviousness is determined. See MPEP §2143 (8th edition, Rev. May 2004). Applicant respectfully submits that when viewed against the framework of this four-step instruction, the rejection of the pending claims over Johnsson, et al. in view of Ko et al. must be withdrawn.

The Office Action states that:

"*Johnson shows an assay of fusion protein reassociation in figure 1e. The assay utilizes fragments of ubiquitin that do not reassociate unless linked to protein domains that have high binding affinity. Upon binding, the ubiquitin fragments are brought into close association and cleave a portion of one of the ubiquitin fragments. The cleavage activity is measured by gel electrophoresis immonoblot analysis in figure 4. Johnsson et al. does not show a fusion protein comprising p53.*

Ko et al. reviews the biology of p53. Ko et al. shows that p53 is a tumor suppressor gene that binds many cellular components, detailed in figure 1 and Table 1. Ko et al. review multiple cellular pathways that p53 appears to play a role in, including apoptosis and cell cycle arrest, differentiation, and DNA repair and replication.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the fusion proteins of Johnsson et al. by use of a fusion protein that comprises p53 because Ko et al. shows that p53 is an important protein involved in tumor suppression that plays a role in multiple cellular pathways and that binds multiple proteins and because use of the protein association assay of Johnsson et al. would allow for interactions of p53 with other proteins to be assayed to allow for further insights into the functions of p53".

The strategy of Johnsson et al. for detecting protein-protein interactions is based on the ubiquitin-based split protein sensor (USPS). The strategy relies on cleavage of proteins with N-terminal fusions to ubiquitin by cytosolic proteases (ubiquitinases) that recognize its tertiary structure. The strategy depends on the reassembly of the tertiary structure of the protein ubiquitin from complementary N- and C-terminal fragments and crucially, on the augmentation of this reassembly by oligomerization domains fused to these fragments. Reassembly is detected as

specific proteolysis of the assembled product by cytosolic proteases (ubiquitinases). Johnson et al. demonstrated that a fusion of a reporter protein-ubiquitin C-terminal fragment could also be cleaved by ubiquitinases, but only if co-expressed with an N-terminal fragment of ubiquitin that was complementary to the C-terminal fragment. The reconstitution of observable ubiquitinase activity only occurred if the N- and C-terminal fragments were bound through GCN4 leucine zippers. Johnson et al suggested that this "split-gene" strategy could be used as an in vivo assay of protein-protein interactions and analysis of protein assembly kinetics in cells. Clearly, the strategy of Johnson et al. requires additional cellular factors (in this case ubiquitinases) and the detection method does not lend itself to high-throughput screening of cDNA libraries.

The Johnsson et al. reference does not teach PCAs' wherein detection of reassembly of the protein fragments is independent of other molecular processes.

Accordingly, to interpret Johnsson et al. for all that it fairly teaches, one of ordinary skill in the art would reasonably conclude that Johnsson et al. does not suggest the desirability of using the assay compositions of the invention for drug discovery.

Ko et al. is not seen to cure the shortcomings of Johnsson et al. The Ko et al. et al reference was relied on for purportedly teaching the biology of p53 and disclosing that p53 is a tumor suppressor gene that binds many cellular components. Also, Ko et al. describes the multiple cellular pathways that p53 appears to play a role in, including apoptosis and cell cycle arrest, differentiation, and DNA repair and replication. Considering the reference for all that it fairly teaches, Ko et al. is simply a review regarding the biology and biochemistry of p53.

Ko et al. fails to teach or suggest the desirability of using the assay composition of the invention and more in particular its use for drug discovery.

None of the compositions or methods are taught or suggested by Ko et al. Further still, Ko et al. does not teach or suggest the many novel assays as presently claimed.

It is respectfully submitted that the combination of cited art fails to set forth a valid prima facie case of obviousness, and withdrawal of the rejection is requested.

It should also be noted that the claims as now amended fully distinguishes the instant claims over Johnsson, et al. The strategy of Johnson et al. requires additional cellular factors (in this case ubiquitinases) while the PCAs' of the invention detection of reassembly of the protein fragments is independent of other molecular processes.

The rejection of claims 2 and 38 under 35 U.S.C. § 103(a) as being unpatentable over copending Application No. 10/856620 (which qualifies as prior art under 35 U.S.C. § 102(f) in view of Panayotou is overcome by the applicants' representative certifying herewith that US pending application 10/856,620 is commonly owned and therefore can not be used as prior art under 35 USC 103(a)/102(f).

In addition the Examiners attention is called to 35 U.S.C. § 103(c) which states that:

(c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

The rejection of claims 2 and 38 under 35 U.S.C. § 103(a) as being unpatentable over

U.S. Patent No. 6,294,330 (which qualifies as prior art under 35 U.S.C.§ 102(f) in view of Panayotou is also overcome by the applicants' representative certifying herewith that US 6,294,330 is commonly owned and therefore can not be used as prior art under 35 USC 103(a)/102(f). See also 35 U.S.C. § 103(c) above.

Claims 2 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,270,964 (which qualifies as prior art under 35 U.S.C. § 102(f) in view of Panayotou. Applicants' representative certifies herewith that US 6,270,964 is commonly owned and therefore can not be used as prior art under 35 USC 103(a)/102(f). See also 35 U.S.C. § 103(c) above.

In determining a prima facie case for obviousness under 35 U.S.C. 103, it is necessary to show that the combination of prior art teachings is proper, and those teachings are sufficient to suggest making the claimed modifications to one of ordinary skill in the art. The distinctions listed above between the currently amended claims and Johnsson et al. are not described in Ko et al. or Panayotou hence the 103 rejections are overcome.

Accordingly, Applicants submit that all the rejections of 1-5 under 35 U.S.C. 103(a) are improper for each, and certainly for all, of the above reasons. Applicants respectfully request reconsideration and withdrawal of the rejection, and an early indication of the allowance of these claims.

DOUBLE PATENTING

Applicant is filing herewith two terminal disclaimers. One terminal disclaimer disclaims the term the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of prior commonly owned

U.S. Patent Nos. 6,270,964; 6,294,330 and 6,428,951.

The other terminal disclaimer disclaims, the terminal part of the statutory term of any patent granted on the instant application, which would extend beyond the expiration date of the full statutory term of any patent granted on commonly owned pending reference Application Numbers 10/856,620 filed May 29, 2004; 10/724,178 filed February 5, 2004; 10/353,090 filed January 29, 2003; 10/154,758 filed May 24, 2002; and 09/603,885 filed June 26, 2000.

The rejection of claims 2 and 38 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-5 of copending Application No. 10/865620 in view of Panayotou et al. is also believed to be overcome by the terminal disclaimers being filed simultaneously with this amendment.

Claims 2 and 38 stand rejected under the judicially created doctrine of obvioussnes-type double patenting as being unpatentable over claims 3, 4, and 13-22 of U.S. Patent No. 6,294,330 in view of Panayotou et al. The enclosed terminal disclaimers obviate this rejection.

The rejection of claims 2 and 38 under the judicially created doctrine of obvioussnes-type double patenting as being unpatentable over claims 27 and 37 of U.S. Patent No. 6,294,330 in view of Panayotou et al. is believed to be overcome by the terminal disclaimers being filed simultaneously with this amendment.

THE REJECTION UNDER 35 USC § 102(f)

The Examiners' attention is called to the enclosed declaration under 37 C.F.R. § 1.132 which would obviate all the rejections under 35 U.S.C § 102(f).

SUMMARY AND CONCLUSION

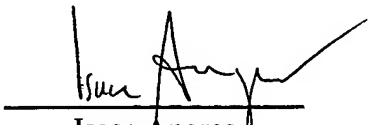
Entry and consideration of the present amendment, reconsideration of the outstanding office action rejections and objections, and allowance of the present application and all of the claims therein are respectfully requested and now believed to be appropriate.

Any amendment to the claims that have been made in this amendment, which do not narrow the scope of the claims, and which have not been specifically noted to overcome a rejection based upon the prior art, should be considered cosmetic in nature, and to have made for a purpose unrelated to patentability, and no estoppel should be deemed to attach thereto.

In view of the above amendments and remarks, it is respectfully submitted that the claims are now in condition for allowance. The Examiner is invited to contact the undersigned at 703-418-2777 if he feels that further discussion may facilitate the resolution of any outstanding issues.

An early indication of a Notice of Allowance is earnestly solicited.

Respectfully submitted,



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